REMARKS

Status of the Claims.

Claims 1-23 are pending in the application.

Election/Restriction.

In the Restriction Requirement, the Examiner restricted the claims under 35 U.S.C. § 372, and 35 USC 121, requiring Applicants to elect one of the following claim groups for prosecution in the present application:

I. Claims 1-6, ...drawn to methods of producing a derivatised antibody . . . .

II. Claims 7-21, and 23 ...drawn to a derivatised antibody and medicament. . . .

III. Claims 22, ...drawn to method of diagnosis, said method comprising exposing a patient to a derivatised antibody . . .

Office Action, at page 2.

Applicants hereby elect proposed Group I (claims 1-6), with traverse.

The Invention Does Not Lack Unity of Invention

The restriction requirement is traversed because Groups I, II and III do not lack a unity of invention. According to the MPEP § 823, and § 1850, "[a]ny international application [or national stage application] must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (PCT Article 3(4)(iii) and 17(3)(a), PCT Rule 3.1, and 37 CFR 1.475)." *See also*, MPEP § 1893.03(d) and 37 CFR 1.499. "Unity of invention exits only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term 'special technical features' is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings." MPEP § 1850 and Rule 13.2 PCT.

Applicants submit that the three groups (Group I, Group II and Group III) identified by the Examiner do relate to a single general inventive concept under Rule 13.1 PCT. The stable flipped-out carbohydrate conformation of the derivatised antibodies (and their consequent ability to interact with carbohydrate groups of adjacent molecules) constitutes a special technical feature as required by Rule 13.2 PCT.

The Examiner's assertion of lack of unity of invention appears to be based on a misunderstanding by the Examiner. The Examiner asserts that "the claimed property of being 'capable of binding immobilized IgG,' is due to the thiolation of the antibodies" and that as a result, "the thiolated antibodies of the prior art meet the limitations of the antibody of the instant claims". Action at page 2, citing U.S. Patents Nos. 5,191,066, 5,597,569, 5,684,137 and/or 6,139,869. However, this is not the case.

The steps of the method of claims 1 to 6 have two distinct elements. The precursor antibody must be (i) treated "to expose a carbohydrate chain...from an interstitial site on the surface of the precursor antibody" and (ii) derivatised. The Examiner appears to be overlooking the element in the claim "to expose a carbohydrate chain... *from an interstitial site*," which is significant here (emphasis added).

Although eukayotically-expressed antibodies are all typically glycosylated, this does not mean that the carbohydrate residues of all antibodies in the prior art are exposed as recited in the claims. The invention provides that carbohydrate chains of antibodies sit in interstitial sites in the folded polypeptide surface of the antibody and can be induced to flip out from these interstices by suitable treatment (e.g. in suitable buffers). This exposes "cryptic" amino acid residues normally masked by the carbohydrate, which can then be chemically derivatised. This derivatisation sterically prevents the carbohydrate chains from returning to their original positions in the interstices of the polypeptide surface. Thus, the claimed methods result in antibodies that are stabilized in the "exposed" conformation. This is described in the specification, *inter alia* at page 22, lines 12 to 24 of the international application WO 99/41286.

As a result, the interstices on the antibody surface to which the carbohydrate would normally bind are now free to interact with other carbohydrate residues, e.g. from adjacent antibodies, hence the stacking properties of the derivatised antibodies (Figure 7; page 23, final paragraph).

The cited paragraph on page 22 also describes Figures 4 and 5 of the application, which show that simple thiolation is not sufficient to produce stackable HIG. See page 22, lines 9-29 of the application. This is because the carbohydrate chains remain throughout the reaction in the surface interstices, which are therefore not exposed either during or after thiolation. Likewise, none of the prior art cited describes thiolation conditions which would produce the flipped-out, exposed carbohydrate chains required for Applicants invention. Thus, in the prior art methods the carbohydrate chains would remain in their normal interstitial conformation during thiolation, there would be no derivatisation of the cryptic amino acid residues as required to stabilize the flipped-out conformation (these amino acids would be shielded throughout by the carbohydrate residues) and so the thiolated antibodies of the prior art would not display the stacking behavior of the antibodies made by the claimed methods. Thus, the thiolated antibodies of the prior art do not meet the requirements of the present claims.

In addition, as stated in 37 CFR 1.475, and MPEP § 1850, unity of invention can exist with combinations of different categories of claims if specific combinations of inventions are present, which include the following: 1) a product and a special process of manufacture of said product; 2) a product and a process of use of said product; 3) a product, a special process of manufacture of said product, and a process of use of said product; 4) a process and an apparatus specially designed to carry out said process; and 5) a product, a special process of manufacture of said product, and an apparatus specially designed to carry out said process. Furthermore, "[a] process is 'specially adapted' for the manufacture of a product if the claimed process inherently produces the claimed product with the technical relationship being present between the claimed process and the claimed product. The expression 'specially adapted' does not imply that the product could not also be manufactured by a different process." MPEP § 1893.03(d).

Applicants' application is drawn to methods, products and process using the products of derivatised antibodies that possess the characteristics as described above as specific combination number 3. Specifically, claims 1 to 6 are directed to a method of derivatising an antibody (a special process for the manufacture of a product); claims 7 to 21 and 23 are directed to the derivatised antibody made by the method of claim 1 (product) and use of the derivatised antibody (process of use of the product); and claim 22 is directed to the diagnostic use of these derivatised antibodies (process of use of the product). As described above, the precursor

antibody must be (i) treated "to expose a carbohydrate chain...from an interstitial site on the surface of the precursor antibody" and (ii) derivatised. This provides the technical relationship between the product (a derivatised antibody), the special process of manufacture of the derivatised antibody and the process of use of the derivatised antibody. As a result, it can be seen that the claimed method, and products of the claimed methods (claims 7-21, 22) or use of the product of the claimed method (23) are in fact novel and non-obvious *per se*. Therefore, the recitation of the process in the product claims does lend patentable weight to these claims because the products of those processes are novel and non-obvious in their own right. Since there is at least one common or corresponding technical feature in the different proposed categories of claims (process, product and process of use) and the Examiner has failed to cite any art to the contrary regarding this technical feature, Applicants' invention has unity of invention and the restriction requirement should be withdrawn.

If at all, Linking Claim Restriction Practice Should Be Applied

Applicants submit that even if the Examiner improperly maintains the lack of unity of invention, the Examiner still must apply linking claim restriction practice in this case. The restriction requirement would then be properly conditioned on the nonallowance of any linking claims. *See* MPEP § 809.04. According to the MPEP §809.03, "[t]here are a number of situations which arise in which an application has claims to two or more properly divisible inventions, so that a requirement to restrict the application to one would be proper, but presented in the same case are one or more claims (generally called 'linking' claims) inseparable therefrom and thus linking together the inventions otherwise divisible. The most common types of linking claims which, if allowed, act to prevent restriction between the inventions that can otherwise be shown to be divisible, are (A) genus claims linking species claims; (B) a claim to the necessary process of making a product linking proper process and product claims; (C) a claim to 'means' for practicing a process linking product apparatus and process claims; and, (D) a claim to the product linking a process of making and a use (process of using)."

Claim 1 (and its dependent method claims 2-6) is drawn to a method of producing a derivatised antibody. Claim 7 (and its dependent claims 8-17) is drawn to a derivatised antibody made by the method of claim 1, while dependent claims 18-21 are drawn to a medicament comprising the derivatised antibody of claim 7 made by the method of claim 1.

Claim 22 is drawn to a method for the in vivo diagnosis of a condition associated with immobilised IgG using the derivatised antibody of claim 7, which is made, by the method of claim 1. Finally, claim 23 is drawn to a pharmaceutical composition comprising a derivatised antibody made by the method of claim 1. Claim 1 is a linking claim to claims 7-23. Claim 1 is "a claim to the necessary process of making a product linking proper process and product claims" as described above in MPEP § 809.03 (B). Thus, even if the Examiner improperly maintains the rejection for lack of unity, the dictates of the MPEP at § 809.03(B) must be followed. A linking claim restriction is contingent on the allowance of the linking claim. The Examiner has presented no evidence that the linking claims are not allowable. As a result, the restriction requirement must be withdrawn.

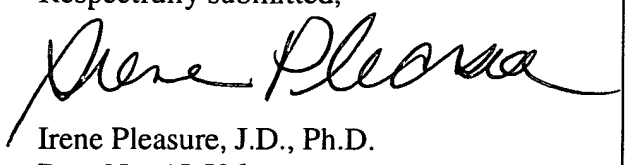
CONCLUSION

Because the invention does not lack unity of invention for at least the reasons above, Applicants respectfully request that the restricted groups be re-joined and co-examined. In the Restriction Requirement, the Examiner also required that if either Group II or III is elected, Applicants also needed "to elect a specific autoimmune disorder for which the claimed antibody provides a diagnosis or treatment, such as one listed in claim 16." Action at page 3. Should the Groups be re-joined as requested by the Applicants, Applicants elect species "rheumatoid arthritis."

In the event that the requirement is maintained, Applicants have elected, with traverse, that claims 1-6 (Examiner's Group I) be examined in the present invention. Applicants expressly reserve the right to petition the restriction requirement prior to any appeal, as provided for at 37 C.F.R. § 1.144.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

Respectfully submitted,



Irene Pleasure, J.D., Ph.D.
Reg. No. 45,506

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P.O. BOX 458
Alameda, CA 94501
(510) 337-7871
Fax (510) 337-7877